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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,040	07/18/2006	Isabelle Meynil-Salles	2912956-029000	8536
84331	7590	04/30/2010	EXAMINER	
Baker Donelson Bearman, Caldwell & Berkowitz, PC			PAK, YONG D	
555 Eleventh Street, NW, Sixth Floor				
Washington, DC 20004			ART UNIT	PAPER NUMBER
			1652	
			NOTIFICATION DATE	DELIVERY MODE
			04/30/2010	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/585,040	MEYNIAL-SALLES ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	YONG D. PAK	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 22 January 2010.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-6,9-14,16,17,22-27,30-36 and 39-49 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-6, 9-14, 16-17, 22-27, 30-36, and 39-49 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                         | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|  | 6) <input type="checkbox"/> Other: _____ .                        |

## **DETAILED ACTION**

This application is a 371 of PCT/FR05/00070.

The amendment filed on January 22, 2010 has been entered.

Claims 1-6, 9-14, 16-17, 22-27, 30-36, and 39-49 are pending and are under consideration.

### ***Response to Arguments***

Applicant's amendment and arguments filed on January 22, 2010, have been fully considered and are deemed to be persuasive to overcome some of the objections/rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Claim Objections***

In view of the amendment, the objections to claims 1, 16, 17, 22, and 46 have been **withdrawn**.

### ***Claim Objection***

Claims 16 and 34 are objected to because of the following informalities:

Claim 16 is objected to because the claim does not have a period after "claim 1".

Claim 36 is objected to because the claim recites "pj/A, pj/B" instead of "pf/A, pf/B".

Appropriate corrections are requested.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In view of the amendment and applicants arguments, the rejection of claims 1, 10, 12, and 16 and claims 2-14, 17, and 32-49 depending therefrom for the recitation of the phrases “Evolved microorganisms”, “cause evolution”, “evolved genes”, and “Evolved strain” under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn**.

In view of the amendments and applicants argument, the rejection of claims 1 and 12 and claims 2-13, 14, 17, and 32-49 depending for the recitation of the phrase “improved” under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn**.

In view of the amendment, the rejection of claims 4, 7-10, 26-29, and 35-39 for the recitation of the phrase “favours” under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn**.

In view of the amendment, the rejection of claims 6 and 27 for the recitation of the phrase “low sensitivity to inhibition by NADH” under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn**.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 9-14, 16-17, 22-27, 30-36, and 39-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-6, 9-14, 16-17, 22-27, 30-36, and 39-49 are drawn to a strain of evolved microorganism, bacterium, *Escherichia* and *Corynebacterium* comprising **(A)** a deletion of the *tpiA* gene and deletion of at least one gene involved in conversion of methylglyoxal into lactate or deletion of *gloA*, *aldA*, *aldB*, *ldhA*, *pflA*, *pflB*, *adhE*, and/or *edd*, wherein said strain having an improved synthesis of 1,2-propanediol, **(B)** said strain of (A) comprising exogenous genes encoding enzymes that favor the metabolism of pyruvate to acetate and/or pyruvate to acetyl-CoA and NADH, **(C)** said strain of (A) comprising exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone, and **(D)** a method of preparing said strain of

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(A), (B) or (C). Therefore, these claims encompass a strain of any or all microorganism, bacterium, yeast, fungus, *Escherichia* and *Corynebacterium* comprising **(A)** a deletion of the *tpiA* gene and deletion of any or all genes involved in conversion of methylglyoxal into lactate or deletion of *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd*, wherein said strain having an improved synthesis of 1,2-propanediol, **(B)** said strain of (A) comprising any or all genes encoding enzymes that favors the metabolism of pyruvate to acetate and/or pyruvate to acetyl-CoA and NADH, **(C)** said strain of (A) comprising any or all exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone, and **(D)** a method of preparing said strain of (A), (B) or (C). Therefore, these claims are drawn to a genus of any or all microorganism, bacterium, *Escherichia* and *Corynebacterium* comprising a deletion of the *tpiA* and any gene involved in conversion of methylglyoxal into lactate, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* and comprising any or all exogenous genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and any or all exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone, wherein said strain has an improved synthesis of 1,2-propanediol. The specification describes an *E. coli* comprising deletions of its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd*, wherein said *E. coli* has improved 1,2-propanediol synthesis. However, the specification does not provide an actual reduction to practice of the claimed microorganism because the specification fails to disclose (1) the structure of *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd*, genes in non-E. coli, which must be known in order to inactivate said genes in the

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claimed microorganism, (2) the structure of genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and (3) the structure of genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone, wherein said claimed microorganism comprises any or all microorganism, bacterium, *Escherichia* and *Corynebacterium*, wherein its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes are deleted and expresses any or all exogenous genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and any or all exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone. The specification does not disclose the isolation or cloning of any non-*E. coli* *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd*, genes. The specification does not describe any structural features of non-*E. coli* *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd*, genes that would have been expected to be shared by other any or all microorganism, bacterium, *Escherichia* and *Corynebacterium* *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes. The level of knowledge and skill in the art does not allow those skilled in the art to structurally envisage or recognize any or all microorganism, bacterium, *Escherichia* and *Corynebacterium* *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes and any or all exogenous genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and any or all exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone because it is known that corresponding genes in different species tend to differ in sequence and the amount and type of sequence

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variation is unpredictable. Since the structure of the *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes would be expected to vary unpredictable from the structure of *E. coli* *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes, the disclosed *E. coli* strain comprising deletion of its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* do not constitute a representative number of species to describe the whole genus of any or all microorganism, bacterium, *Escherichia* and *Corynebacterium* comprising deletion of *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes and there is no evidence on the record of the relationship between the structure of the disclosed *E. coli* strain and the structure of any or all microorganism, bacterium, *Escherichia* and *Corynebacterium* comprising deletion of *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes and expressing any or all exogenous genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and any or all exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone. Because the *E. coli* strain comprising deletion of its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes is not representative of the entire claimed genus, and the specification does not disclose structural features shared by members of the genus, the description of the modified *E. coli* comprising deletion of its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes and expressing any or all exogenous genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and any or all exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone would not have put the application in possession of the

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common structural attributes or features shared by members of the genus that structurally distinguish the members of the genus from other materials at the time of filing. Thus, the description of the *E. coli* comprising deletion of its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes is not sufficient to describe the claimed genus of any or all microorganism, bacterium, *Escherichia* and *Corynebacterium* comprising deletion of its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes and expressing any or all exogenous genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and any or all exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone. Accordingly, the specification does not provide a representative number of species or sufficient common structural features to show that the application would have been in possession of the claimed genus as a whole at the time of fling. Therefore, the specification fails to describe a representative species of the genus comprising any or all yeast or genus comprising any or all microorganism, bacterium, *Escherichia* and *Corynebacterium* comprising comprising deletion of its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes and expressing any or all exogenous genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and any or all exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that

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applicants were in possession of the inventions of claims 1-6, 9-14, 16-17, 22-27, 30-36, and 39-49.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the rejection has been overcome because the claims have been amended to recite the use of the invention with bacterium, specifically *E. coli* and *Corynebacterium*. Examiner respectfully disagrees. First, the claims are not limited to the use of *E. coli*. Second, the specification does not provide an actual reduction to practice of the claimed microorganism because the specification fails to disclose (1) the structure of *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd*, genes in non-E. coli, which must be known in order to inactivate said genes in the claimed microorganism, (2) the structure of genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and (3) the structure of genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone, wherein said claimed microorganism comprises any or all microorganism, bacterium, *Escherichia* and *Corynebacterium*, wherein its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes are deleted and expresses any or all exogenous genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and any or all exogenous genes encoding an enzymes that are involved in the

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conversion of acetyl-CoA and acetate into acetone. The specification does not disclose the isolation or cloning of any non-*E. coli* *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd*, genes. Because the *E. coli* strain comprising deletion of its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes is not representative of the entire claimed genus, and the specification does not disclose structural features shared by members of the genus, the description of the modified *E. coli* comprising deletion of its *tpiA*, *gloA*, *aldA*, *aldB*, *IdhA*, *pflA*, *pflB*, *adhE*, and/or *edd* genes and expressing any or all exogenous genes encoding enzymes that favors the metabolism of pyruvate to acetate, acetyl-CoA and NADH and any or all exogenous genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone would not have put the application in possession of the common structural attributes or features shared by members of the genus that structurally distinguish the members of the genus from other materials at the time of filing.

Hence the rejection is maintained.

***Claim Rejections - 35 USC § 102***

In view of the amendment, the rejection of claims 1-3, 5-9, 13-14, 16, 22-24, 26-33, 35-39, and 42-43 under 35 U.S.C. 102(b) as being anticipated by Cameron et al., has been **withdrawn**.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 5-6, 9-14, 16, 22-24, 26-27, 30-32, 35-36, 39-46, and 48-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cameron et al., Altaras et al. and Bermejo et al.

Claims 1-2, 5-6, 9-14, 16, 22-24, 26-27, 30-32, 35-36, 39-46, and 48-51 drawn to an *E. coli* comprising a deletion of its *tpiA*, *gloA*, and *ldhA* genes and comprising evolved genes encoding enzymes that increases synthesis of 1,2-propanediol and a method of producing said *E. coli*.

Cameron et al. (US Patent No. 6,303,352 B1 – cited previously on form PTO-892) discloses a method of modifying or “evolving” *E. coli* to increase production of 1,2-

propanediol by deleting its *tpiA* and/or *gloA* genes and over-expressing genes encoding enzymes that increases metabolism of pyruvate to acetate and/or pyruvate to acetyl-CoA and NADH, wherein said *E. coli* has improved 1,2-propanediol synthesis, and a method of producing said *E. coli* (Column 4, line 66 through Column 12, line 16). *E. coli* has an endogenous pyruvate dehydrogenase complex.

The difference between the reference of Cameron et al. and the instant invention is that the reference of Cameron et al. does not teach deletion of *ldhaA* and expression of *C. acetobutylicum* gene encoding an enzyme that increases production of acetone.

Altaras et al. (Biotechnol. Prog. 16:940-946 - form PTO-1449) discloses enhanced production of 1,2-propanediol by deleting *ldhaA* gene in *E. coli* (abstract and page 940). Altaras et al. teaches that elimination of the byproduct, lactate, increases production of 1,2-propanediol (abstract and page 940).

Bermejo et al. (Appl Environ Microbiol. 1998 Mar;64(3):1079-85 - form PTO-892) discloses expression of *C. acetobutylicum* gene encoding an enzyme that increases production of acetone in *E. coli* in order to improve solvent production and an acetone producing *E. coli* may be useful hosts, which decreases the accumulation of detrimental acetate (page 936).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a recombinant *E. coli* by deleting it's *tpiA*, *gloA*, *ldhA* genes and over-express a *C. acetobutylicum* gene encoding an enzyme that decreases accumulation of acetate. One of ordinary skill in the art at the time the invention was made would have been motivated to do the above for the purpose of

eliminating production of the byproduct, lactate, and in order to increase production of 1,2-propanediol and decrease accumulation of acetate. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for success sine Cameron et al. teaches deletion of the *tpiA* and *gloA* gene in *E. coli* to increase 1,2-propanediol production, Altaras et al. teaches deletion of *ldhA* gene in *E. coli*, which results in increased production of 1,2-propanediol and Bermejo et al. teaches expression of a *C. acetobutylicum* gene encoding an enzyme that increases production of acetone in *E. coli* in order to decrease accumulation of acetate.

Therefore, the above references render claims 1-6, 9-14, 16, 22-27, 30-36, 39-46, and 48-51 *prima facie* obvious.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that Cameron et al. do not teach the elements of the independent claims and teaches away from the instant invention because in order to have non-native PD production, one would need to have at least the TP ( $\Delta tpi$ ) mutant transformed with any number of exogenous genes. Examiner respectfully disagrees. The claims are not limited to only evolving endogenous genes involved in the biosynthesis of 1,2-propanediol from DHAP and methylglyoxal or deleting genes that reduce the availability of methylglyoxal for 1,2-propanediol. Cameron et al. discloses a method of modifying or “evolving” *E. coli* to increase production of 1,2-propanediol by deleting its *tpiA* and/or *gloA* genes. Also, the instant rejection is based on the combined teachings of Cameron et al., Altaras et al. and Bermejo et al.

Applicants also argue that Altara et al. teaches away from the present invention because Altara et al.'s disclosure of a complete pathway eliminates the need to rely on the host's native genes and regulations to synthesize the desired enzymatic activities and Altara et al. reinforces Cameron that the solution to the production of 1,2-propanediol in microorganism is identified as requiring the introduction of exogenous genes. Examiner respectfully disagrees. Altaras et al. discloses enhanced production of 1,2-propanediol by deleting the *ldhaA* gene in *E. coli* (abstract and page 940). Altaras et al. teaches that elimination of the byproduct, lactate, via deletion of the *ldahA* gene increases production of 1,2-propanediol (abstract and page 940).

Applicants also argue that Altara et al. does not mention *tpiA*. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The reference of Cameron et al. is relied upon for its teaching of deletion of the *tpiA* gene in *E. coli*.

Applicants argue that Bermejo et al. does not rectify the deficiencies of Cameron et al. and Altara et al. because Bermejo is solely concerned with the transfection of *E. coli* with a gene encoding a protein that converts acetate into acetone and Bermejo et al. does not disclose deletion of the *tipA* gene nor any other gene in the MG to lactate pathway. As discussed above, Cameron et al. and Altara et al. disclose deletion of the *tipA* gene and other genes in the MG to lactate pathway. The reference of Bermejo et

al. is relied upon for its teaching of a polynucleotide encoding an enzyme that increases production of acetone from acetate, which can be expressed in *E. coli* in order to decrease accumulation of acetate that is detrimental to *E. coli*.

Hence the rejection is maintained.

### ***Conclusion***

None of the claims are in condition for allowance.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/  
Primary Examiner, Art Unit 1652